Remarks

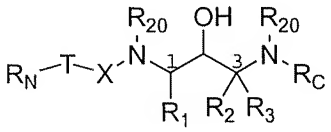
Claims 1, 3-19, 21, 22, and 24 are currently pending. Claim 22 stands withdrawn. No amendments are made herein.

Rejections based on 35 U.S.C. § 102(e)

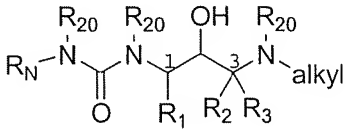
a. Claims 1, 3-18, 21,and 24 stand rejected under §102(e) as being anticipated by Fobian et al., WO 2004022523 ("Fobian").

Applicants respectfully submit that "[t]o anticipate a claim, the reference must teach every element of the claim." MPEP 2131 page 2100-76. Fobian lacks elements required by the claims and, therefore, does not anticipate the claims under 102.

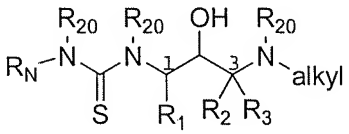
In particular, the instant claims are directed to compounds of formula



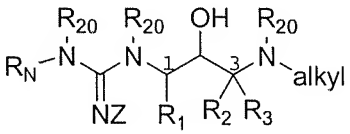
wherein X is -(C=O)-, -(C=S)-, or -(C=N-Z)-; T is NR_{20}; and R_C is, generally, optionally substituted alkyl, aryl, heteroaryl, or cycloalkyl. The resulting formulae can be represented by the following structures respectively for the urea, thiourea, and guanidine containing compounds of the instant invention.



Urea



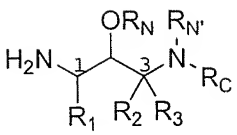
Thiourea



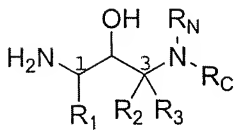
Guanidine

Therefore, the instant claims require a 2-hydroxypropyl group substituted with a urea, thiourea, or guanidine group at carbon 1 and an amine group at carbon 3.

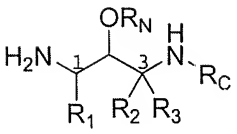
Fobian discloses compounds of generic structure (AA), (I), (X), and (Y), at pages 5, 20, 29, 29, and 34, respectively:



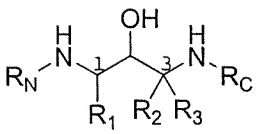
(AA)



(I)



(X)



(Y)

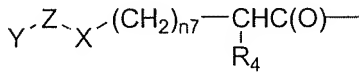
Structures (AA), (I), and (X) teach substitution of a 2-hydroxypropyl core with an NH_2 group at carbon 1. Formulae (AA), (I), and (X) do not encompass a urea, thiourea, or guanidine at carbon 1. Therefore, formulae (AA), (I), and (X) do not teach every element of the instant claims and consequently do not anticipate the instant claims.

With regard to formula (Y), the Fobian specification, at page 5, defines R_N as:

$-C(=O)-(CRR')_{0-6}R_{100}$, $-C(=O)-(CRR')_{1-6}-O-R'_{100}$,

$-C(=O)-(CRR')_{1-6}-S-R'_{100}$, $-C(=O)-(CRR')_{1-6}-C(=O)-R_{100}$,

$-C(=O)-(CRR')_{1-6}-SO_2-R_{100}$, $-C(=O)-(CRR')_{1-6}-NR_{100}-R'_{100}$, or



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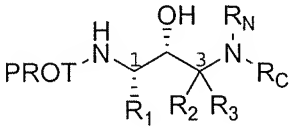
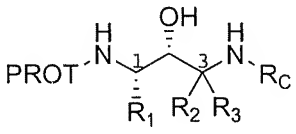
Formula (Y) teaches only amide substituents at carbon 1. Applicants note that $-C(=O)-(CRR')_{0-6}R_{100}$ may reduce to $-C(=O)R_{100}$. The Fobian specification does not define R_{100} as an amino group, which is necessary to teach ureas. Formula (Y) does not teach every element of the instant claims and, therefore, formula (Y) does not anticipatory.

Fobian describes "intermediates" of formula (IA) and (VII) at pages 112 and 349-350, respectively:



(IA)



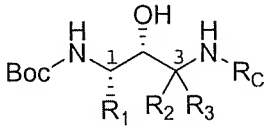
(VII)

wherein PROT is defined as "an amine protecting group" at page 113. The Fobian specification discloses "suitable" amine protecting groups as, generally, carbamates and amides, and to a

lesser extent, silyl, allyl, and arylalkyl groups. The Fobian application does not include ureas, thioureas, or guanidines as amine protecting groups. Further, it is well known by those skilled in the art that ureas, thioureas, and guanidines are not considered amine protecting groups.

Generally, formulae (IA) and (VII) teach a 2-hydroxypropyl core substituted with a carbamate or amide at carbon 1. Specifically, formulae (IA) and (VII) do not teach a 2-hydroxypropyl core substituted with a urea, thiourea, or guanidine at carbon 1. Therefore, formulae (IA) and (VII) do not anticipate the instant claims.

Finally, Fobian provides "preparations" at pages 170-179 that are carbamates represented by the formula



wherein Boc, at page 136, is defined as "t-butoxycarbonyl." Thus, the "preparations" section in Fobian teaches a 2-hydroxypropyl core substituted with a tert-butyl carbamate. The formula above does not disclose a 2-hydroxypropyl core substituted with a urea, thiourea, or guanidine. Therefore, Fobian does not anticipate the instant claims.

Fobian teaches, generally, a 2-hydroxypropyl core substituted with an NH_2 group, carbamate group, or an amide group. Specifically, Fobian, does not teach a 2-hydroxypropyl group substituted with a urea, thiourea, or guanidine. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

Finally, Applicants note that the Office cites a priority date for Fobian based on a provisional application filed September 06, 2002. However, the Office has not asserted that the subject matter of the pending claims is disclosed in the

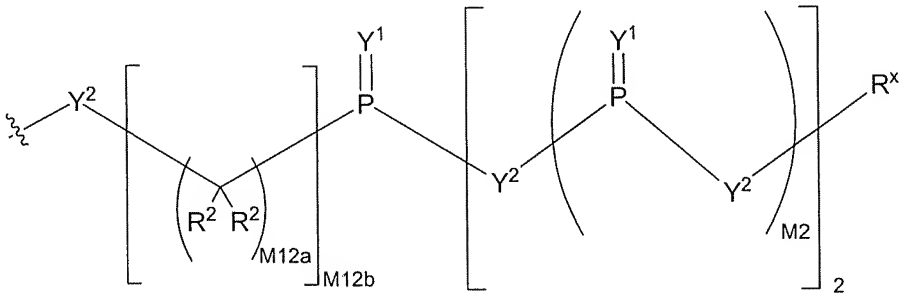
priority document for Fobian. Accordingly, since Applicants' priority application, which does describe the subject matter of the instant claims, predates the filing date of Fobian, the instant claims are not anticipated by the reference.

b. Claims 1, 3-18, 21,and 24 stand rejected under §102(e) as being anticipated by Birkus et al., WO 2003090691 ("Birkus").

As noted above, a reference must teach every element of the claims to be anticipatory. Applicants respectfully submit that Birkus lacks elements required by the claims and, therefore, does not anticipate the claims under 102.

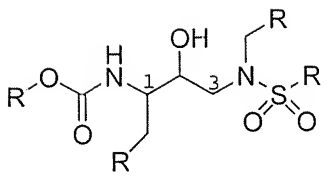
As pointed out above, the instant claims require a 2-hydroxypropyl group substituted with a urea, thiourea, or guanidine group at carbon 1 and an amine group at carbon 3.

Birkus teaches the substitution of HIV-active compounds with an ester or phosphonate group to improve pharmacologic properties. The Birkus phosphonate groups are described by formula

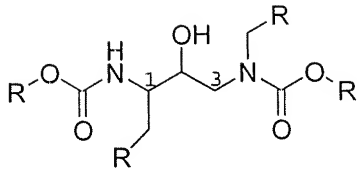


Clearly, the broad language and formula found in Birkus does not teach every element of the instant claims.

The Birkus specification, at pages 299-652, 729-761, 777, and 791, discloses a variety of compounds generally encompassed by formulae:



and



wherein each R group independently represents a wide variety of substituents.

The Birkus compounds have a 2-hydroxypropyl core disubstituted with a carbamate group and a sulfonamide group, or a 2-hydroxypropyl core disubstituted with two carbamate groups. None of the Birkus compounds contain a 2-hydroxypropyl group substituted with a urea, thiourea, or guanidine. Therefore, Birkus does not teach every element of the instant claims and is not anticipatory. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

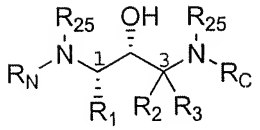
Applicants note that the Office cites a priority date for Birkus based on a provisional application filed April 26, 2002. However, the Office has not asserted that the subject matter of the pending claims is disclosed in the priority document for Birkus. Accordingly, since Applicants' priority application, which does describe the subject matter of the instant claims, predates the filing date of Birkus, the instant claims are not anticipated by the reference.

Rejection based on 35 U.S.C. § 102(a)

Claims 1, 3-18, 21, and 24 stand rejected under §102(a) as being anticipated by John et al., WO 2003040096 ("John").

As stated above, a reference must teach every element of the claims to be anticipatory. Applicants respectfully submit that John lacks elements required by the claims and, therefore, does not anticipate the claims under 102.

In particular, John teaches compounds of formula X:



X

wherein R_N is defined by the John specification, at page 9, as:

R'_{100}, $-SO_2R'_{100}$, $-(CRR')_{1-6}R'_{100}$, $-C(=O)-(CRR')_{0-6}R_{100}$,

$-C(=O)-(CRR')_{1-6}-O-R'_{100}$, $-C(=O)-(CRR')_{1-6}-S-R'_{100}$,

$-C(=O)-(CRR')_{1-6}-C(=O)-R_{100}$, $-C(=O)-(CRR')_{1-6}-SO_2-R_{100}$, or

$-C(=O)-(CRR')_{1-6}-NR_{100}-R'_{100}$.

Formula X teaches amine, amide and sulfonamide substituents at carbon 1. The John specification discloses approximately 3980 examples in support of amine, amide, sulfonamide, and carbamate substituents at carbon 1. Formula X does not teach urea, thiourea, or guanidine groups at carbon 1. John does not teach all the elements of the instant claims and, therefore, John is not anticipatory.

Further, Applicants note that the instant invention's priority date of November 27, 2002 precedes the John reference's publication date of May 15, 2003. The Office contends that the above argument is not persuasive because "[John] et al., was published before the filing date of the instant invention and [John} et al., provisional application, US2001-337122P, was filed, November 08, 2001. Applicants are confused by the Examiner's contention and respectfully request clarification.

The statutory language provides that:

> "[a] person shall be entitled to a patent unless the invention was known of used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent." 35 U.S.C. § 102(a).

The MPEP provides:

> "[f]or 35 U.S.C. 102(a) to apply, the reference

> must have a publication date earlier in time than the effective filing date of the application..." MPEP 706.02(a)(II)(C), page 700-26.

The MPEP, citing the Federal Circuit in *Carella v Starlight Archery*, further provides:

> "[t]he statutory language 'known or used by others in this country' (35 U.S.C. § 102(a)), means knowledge or use which is accessible to the public." MPEP 2132(I), page 2100-81.

The instant application's "effective filing date" is November 27, 2002. John published May 15, 2003. The instant application was filed before John was accessible to the public. Therefore, Applicants respectfully submit that John fails to qualify as prior art under 35 U.S.C. § 102(a).

Based on the above discussions, Applicants respectfully request reconsideration and removal of the rejection under 35 U.S.C. § 102(a).

Rejection based on 35 U.S.C. § 103(a)

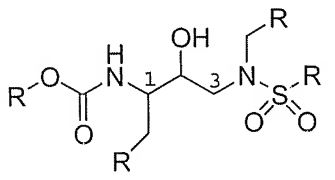
Claims 1, 3-18, 21, and 24 stand rejected as being obvious over "all the prior arts cited above, individually." Applicants respectfully submit that: 1) Fobian and John do not qualify as prior art under 35 U.S.C. 103(c) and 2) Birkus is sufficiently distinguished to overcome the obviousness rejection.

The Supreme Court addressed the standard for determining obviousness in *Grahm v. Deere*:

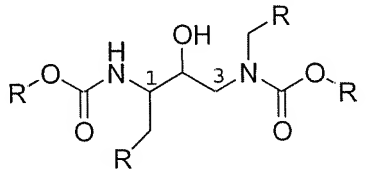
> "[u]nder § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved." 383 U.S. 1, 17-18 (1966)

Scope and content of the Prior Art

Birkus discloses two classes of compounds that are useful for treating HIV. One class comprises a 2-hydroxypropyl core disubstituted with a carbamate and a sulfonamide. A second class of compounds comprises a 2-hydroxypropyl core disubstituted with two carbamates as shown by formulae



and



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Both classes of compounds described above are further substituted with an ester or phosphonate group.

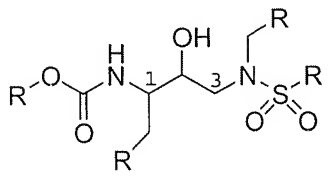
The Differences Between the Prior Art and the Claims

The Office contends that the

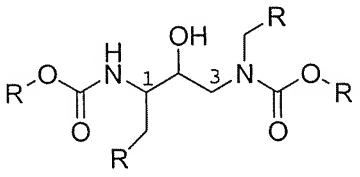
> "difference between the instant invention and that of the prior arts is that Applicant claims H instead of alkyl and vice versa in some of the species embraced by the generic formulae. In other species Applicant claims compounds wherein the length of a carbon chain is either longer or shorter than that of the prior arts."

Applicants respectfully submit that other, more significant, differences exist between Birkus and the instant application.

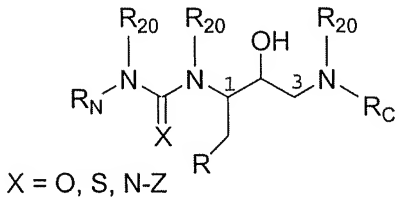
As discussed above, Birkus discloses two general classes of compounds, both of which are significantly different from compounds of the instant invention.



Birkus



Birkus



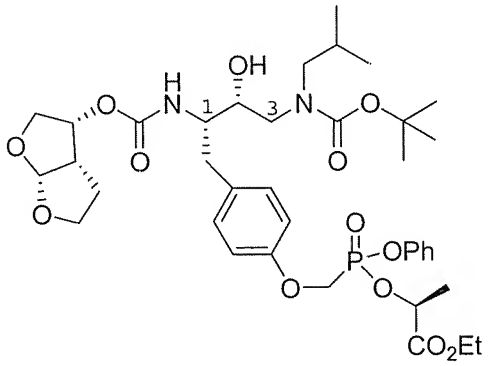
instant application

1) Birkus teaches carbamate substitution at carbon 1. The instant application requires urea, thiourea, or guanidine substitution at carbon 1.

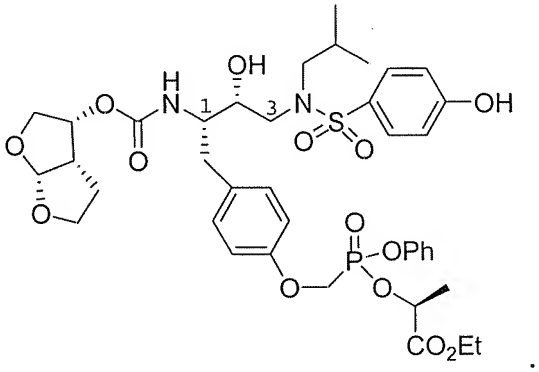
2) Birkus teaches a carbamate or sulfonamide substitution at carbon 3. The instant application requires amine substitution at carbon 3.

3) Birkus teaches that incorporation of an ester or phosphonate group into "any organic compound" with HIV activity improves that activity. The instant application teaches inhibition of beta-secretase by compounds with a 2-hydroxypropyl core substituted with ureas, thioureas, or guanidines at carbon 1 and amines at carbon 3.

For example, Birkus discloses several compounds similar to the structures shown below, pages 493 and 496 respectively:



structure (a)



structure (b)

With regard to structure (a), above, the instant claims:

1) do not encompass carbamates at carbon 1;
2) do not encompass benzyl groups substituted with phosphonates at carbon 1; and
3) do not encompass carbamates at carbon 3;

With regard to structure (b), above, the instant claims:

1) do not encompass carbamates at carbon 1;
2) do not encompass benzyl groups substituted with phosphonates at carbon 1; and

3) do not encompass sulfonamides at carbon 3.

Level of Ordinary Skill in the Pertinent Art

Birkus is of at least ordinary skill in the art and the claimed invention did not occur to them.

Applicants respectfully submit that claims 1, 3-18, 21, and 24 are not obvious in view of Birkus. Birkus discloses several 2-hydroxypropyl compounds substituted with an ester or phosphonate group and either: 1) two carbamate groups or 2) a carbamate group and a sulfonamide group. One skilled in the art would conclude from Birkus that this substitution pattern on 2-hydroxypropyl group is important to the activity desired in Birkus. There is no motivation in Birkus to 1) replace the carbamate group at carbon 1 with a urea, thiourea, or guanidine, 2) replace the carbamate/sulfonamide group at carbon 3 with an amine, and 3) remove the ester or phosphonate group to provide the instantly claimed compounds.

Even if such a suggestion/motivation existed, one skilled in the art would not have a reasonable expectation of success that the modified compounds would possess activity as found in Birkus, or any activity for that matter. One skilled in the art understands that medicinal chemistry is unpredictable. Compounds of the instant invention differ by at least three substantial modifications from the compounds disclosed in Birkus. One cannot predict, nor have a reasonable expectation of success, that multiple modifications will result in active compounds. There is nothing in the Birkus reference that remotely suggests that the claimed compounds would have biological activity. Clearly, the unpredictability of the art in combination with the structural modifications render the instant invention non-obvious.

At best, the Office may consider the modifications, noted above, as obvious to try. The MPEP, however, provides that an "obvious to try rationale in support of an obviousness rejection" is "improper" and "not the standard under § 103." MPEP 2145(X)(B).

Applicants respectfully submit that the instant claims are not rendered obvious by Birkus and request reconsideration and withdrawal of the § 103(a) rejection.

Disqualification of Commonly Owned References Under 103(c)

Section 103(c) provides that subject matter developed by another person, which qualifies as prior art under 102(e) shall not preclude patentability under 103 where the subject matter and claimed invention were, at the time the claimed invention was made, owned by the same person.

With regard to establishing common ownership, the MPEP provides the "following statement is sufficient evidence to establish common ownership of, or an obligation for assignment to, the same person(s) or organization(s):

> Applications and references...will be considered by the examiner to be owned by, or subject to an obligation of assignment to the same person, at the time the invention was made, if the applicant(s) or an attorney or agent of record makes a statement to the effect that the application and the reference were, at the time the invention was made, owned by, or subject to an obligation of assignment to, the same person."
> MPEP 706.02(I)(2)(II) page 700-59.

The instant application and WO 2004022523 (Fobian et al.) were, at the time the invention claimed herein was made, jointly owned by Elan Pharmaceuticals and Pharmacia UpJohn. Applicants

respectfully submit that Fobian is disqualified as prior art under 103(c).

Also, the instant application and WO 2003040096 (John et al.) were, at the time the invention claimed herein was made, jointly owned by Elan Pharmaceuticals and Pharmacia UpJohn. Applicants respectfully submit that John is disqualified as prior art under 103(c).

Rejoinder

Method of use claim 22, currently stands withdrawn from consideration as being drawn to non-elected inventions. However, in accordance with MPEP §821.04(b), if Applicants elect claims directed to a product which is subsequently found allowable, the withdrawn process claims which depend from or otherwise require all the limitations of an allowable product claim will be considered for rejoinder. Upon rejoinder of claims directed to a previously non-elected process invention, the restriction requirement between the elected product and rejoined process claims will be withdrawn. It is submitted that the method claims as presented require all the limitations of the elected product (compound) claims. Thus, if the product claims are found allowable, the non-elected process claims (withdrawn) should be rejoined.

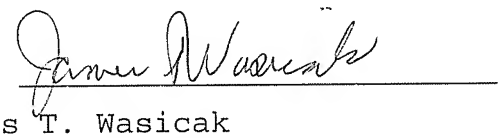
Conclusion

Applicants respectfully submit that the pending claims meet all requirements of patentability. Allowance of the pending claims and passage of the case to issue are therefore respectfully solicited.

Should the Examiner believe a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312) 913-2136.

Respectfully submitted,

Dated: September 29, 2006

By: 

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